AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. **(original):** A method for obtaining a disease-associated gene, wherein a disease-associated transcription factor is expressed in a cell line that is deficient in said transcription factor or in a primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

2. **(original):** A method for obtaining a Runx2/Cbfa1-related disease-associated gene, wherein Runx2/Cbfa1 is expressed in a Runxs/Cbfa1-deficient chondrocyte cell line or in a Runx2/Cbfa1-deficient primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

3. **(currently amended):** A method for obtaining a gene associated with regulation of cartilage differentiation, wherein Runx2/Cbfa1 is expressed in a ~~Runxs/Cbfa1-deficient~~Runx2/Cbfa1-deficient chondrocyte cell line or in a Runx2/Cbfa1-deficient primary cultured cell, and the gene the expression of which is thereby induced or inhibited is screened.

4. **(original):** The method according to any one of claims 1 to 3, wherein said screening is carried out via subtraction or DNA chip analysis.

5. **(original):** A primary chondrocyte or cultured chondrocyte derived from a Runx2/Cbfa1-deficient mouse.

6. **(original):** A chondrocyte derived from a Runx2/Cbfa1- and p53-deficient mouse.

7. **(original):** The chondrocyte cell line derived from the Runx2/Cbfa1- and p53-deficient mouse according to claim 6, which is the RU-1 cell line or the RU-22 cell line deposited under the accession number FERM BP-10137 or FERM BP-10138 at the International Patent Organism Depositary of the National Institute of Advanced Industrial Science and Technology.

8. **(original):** A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, or 25, wherein the expression thereof is induced by Runx2/Cbfa1 expression.

9. **(original):** A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 9.

10. (original): A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1 and encoding a protein capable of stimulating cartilage differentiation.

11. (original): A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 3 and encoding a protein capable of inhibiting cartilage differentiation.

12. (original): A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 5 and encoding a protein capable of stimulating cartilage differentiation.

13. (original): A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 15 and encoding a protein capable of inhibiting cartilage differentiation.

14. (original): A polynucleotide having the nucleotide sequence shown in SEQ ID NO: 25 and encoding a protein capable of inhibiting chondrogenesis.

15. (original): A human homolog polynucleotide of the polynucleotide according to claim 8, which has the nucleotide sequence shown in SEQ ID NO: 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, or 51.

16. (currently amended): A polynucleotide having 65% or more homology to the polypeptide encoded by the polynucleotide <u>having the nucleotide sequence shown in SEQ ID</u>

NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, or 51~~according to any one of claims 8 to 15~~, and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

17. (currently amended): A polynucleotide being capable of hybridizing under stringent conditions to the polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, or 51~~according to any one of claims 8 to 15~~ or a complementary strand thereof, and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

18. (original): A recombinant DNA vector comprising the polynucleotide according to any one of claims 8 to 17 or a complementary strand thereof.

19. (original): A transformant transformed with the recombinant DNA vector according to claim 18.

20. (original): A polypeptide comprising the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52.

21. (original): A polypeptide comprising an amino acid sequence derived from the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52 by deletion, substitution, or addition of one or several amino acid residues, and capable of stimulating or inhibiting cartilage differentiation.

22. (original): A polypeptide comprising an amino acid sequence having at least 65% homology to the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or 52, and capable of stimulating or inhibiting cartilage differentiation.

23. (original): An antisense polynucleotide which regulates the expression of the gene consisting of the polynucleotide according to any one of claims 8 to 17.

24. (original): An RNAi molecule which regulates the expression of the gene consisting of the polynucleotide according to any one of claims 8 to 17.

25. (original): An antibody against the polypeptide according to any one of claims 20 to 22.

26. (original): A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of bringing a candidate compound into contact with a cell that expresses the gene consisting of the polynucleotide according to any one of claims 8 to 17;

(2) a step of assaying the expression level of the gene; and

(3) a step of selecting a compound that lowers or enhances the expression level of the gene compared with a control, which has not been brought into contact with the candidate compound.

27. (original): A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of bringing a cell into contact with a candidate compound, wherein a vector containing the transcription regulatory region of the gene consisting of the polynucleotide according to any one of claims 8 to 17 and a reporter gene expressed under the control of the transcription regulatory region has been introduced into the cell;

(2) a step of assaying activity of the reporter gene; and

(3) a step of selecting a compound that lowers or enhances the expression level of the reporter gene compared with a control, which has not been brought into contact with the candidate compound.

28. (original): A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of administering a candidate compound to a test animal;

(2) a step of assaying the expression level of the gene consisting of the polynucleotide according to any one of claims 8 to 17 in a biological sample obtained from the test animal; and

(3) a step of selecting a compound that lowers or enhances the expression level of the gene compared with the control to which the candidate compound has not been administered.

29. (original): A method for screening for a therapeutic agent and/or prophylactic agent for a bone and/or joint disease comprising the following steps (1) to (3):

(1) a step of bringing a protein encoded by the gene consisting of the polynucleotide according to any one of claims 8 to 17 into contact with a candidate compound;

(2) a step of assaying activity of the protein; and

(3) a step of selecting a compound that lowers or enhances the activity of the protein compared with a control, which has not been brought into contact with the candidate compound.

30. (canceled).

31. (currently amended): A pharmaceutical composition comprising ~~at least one of:~~ the polynucleotide according to any one of claims 8 to 17 and a pharmaceutically acceptable carrier~~; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30~~.

32. (currently amended): A method for preventing and/or treating~~prophylactic agent and/or therapeutic agent for~~ a bone and/or joint disease comprising administering to a subject ~~at least one of:~~ the polynucleotide according to any one of claims 8 to 17~~; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30~~.

33. (currently amended): The method ~~prophylactic agent and/or therapeutic agent~~ according to claim 32, wherein the bone and/or joint disease is osteoarthritis.

34. (currently amended): A method~~composition~~ for diagnosing a disease comprising contacting a sample with ~~at least one of:~~ the polynucleotide according to any one of claims 8 to 17~~; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30~~.

35. (currently amended): A method ~~composition~~ for diagnosing a bone and/or joint disease comprising contacting a sample with~~at least one of:~~ the polynucleotide according to any

one of claims 8 to 17~~; the DNA vector according to claim 18; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30~~.

36. (currently amended): The method ~~composition~~ according to claim 35, wherein the bone and/or joint disease is osteoarthritis.

37. (original): A transgenic animal model of a bone and/or joint disease, in which an expression level of the gene encoded by the polynucleotide according to any one of claims 8 to 17 is enhanced or lowered.

38. (original): A transgenic mouse model of a bone and/or joint disease, in which the gene encoded by the polynucleotide according to any one of claims 8 to 17 is expressed with the use of a type II collagen promoter.

39. (currently amended): A method for preparing an animal model of a bone and/or joint disease comprising administering ~~at least one of:~~ the DNA vector according to claim 18~~; the transformant according to claim 19; the polypeptide according to any one of claims 20 to 22; the antisense polynucleotide according to claim 23; the RNAi molecule according to claim 24; the antibody according to claim 25; and the compound according to claim 30~~.

40. (original): The method for preparing an animal model according to claim 39, wherein the bone and/or joint disease is osteoarthritis.

41. (new): A pharmaceutical composition comprising the DNA vector according to claim 18 and a pharmaceutically acceptable carrier.

42. (new): A pharmaceutical composition comprising the transformant according to claim 19 and a pharmaceutically acceptable carrier.

43. (new): A pharmaceutical composition comprising the polypeptide according to any one of claims 20 to 22 and a pharmaceutically acceptable carrier.

44. (new): A pharmaceutical composition comprising the antisense polynucleotide according to claim 23 and a pharmaceutically acceptable carrier.

45. (new): A pharmaceutical composition comprising the RNAi molecule according to claim 24 and a pharmaceutically acceptable carrier.

46. (new): A pharmaceutical composition comprising the antibody according to claim 25 and a pharmaceutically acceptable carrier.

47. (new): A pharmaceutical composition comprising the compound according to claim 30 and a pharmaceutically acceptable carrier.

48. (new): A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the DNA vector according to claim 18.

49. (new): The method according to claim 48, wherein the bone and/or joint disease is osteoarthritis.

50. (new): A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the transformant according to claim 19.

51. (new): The method according to claim 50, wherein the bone and/or joint disease is osteoarthritis.

52. (new): A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the polypeptide according to any one of claims 20 to 22.

53. (new): The method according to claim 52, wherein the bone and/or joint disease is osteoarthritis.

54. (new): A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the antisense polynucleotide according to claim 23.

55. (new): The method according to claim 54, wherein the bone and/or joint disease is osteoarthritis.

56. (new): A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the RNAi molecule according to claim 24.

57. (new): The method according to claim 56, wherein the bone and/or joint disease is osteoarthritis.

58. (new): A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the antibody according to claim 25.

59. (new): The method according to claim 58, wherein the bone and/or joint disease is osteoarthritis.

60. (new): A method for preventing and/or treating a bone and/or joint disease comprising administering to a subject the compound according to claim 30.

61. (new): The method according to claim 60, wherein the bone and/or joint disease is osteoarthritis.

62. (new): A method for diagnosing a disease comprising contacting a sample with the DNA vector according to claim 18.

63. (new): A method for diagnosing a disease comprising contacting a sample with the transformant according to claim 19.

64. (new): A method for diagnosing a disease comprising contacting a sample with the polypeptide according to any one of claims 20 to 22.

65. (new): A method for diagnosing a disease comprising contacting a sample with the antisense polynucleotide according to claim 23.

66. (new): A method for diagnosing a disease comprising contacting a sample with the RNAi molecule according to claim 24.

67. (new): A method for diagnosing a disease comprising contacting a sample with the antibody according to claim 25.

68. (new): A method for diagnosing a disease comprising contacting a sample with the compound according to claim 30.

69. (new): A method for diagnosing a bone and/or joint disease comprising contacting a sample with the DNA vector according to claim 18.

70. (new): The method according to claim 69, wherein the bone and/or joint disease is osteoarthritis.

71. (new): A method for diagnosing a bone and/or joint disease comprising contacting a sample with the transformant according to claim 19.

72. (new): The method according to claim 71, wherein the bone and/or joint disease is osteoarthritis.

73. (new): A method for diagnosing a bone and/or joint disease comprising contacting a sample with the polypeptide according to any one of claims 20 to 22.

74. (new): The method according to claim 73, wherein the bone and/or joint disease is osteoarthritis.

75. (new): A method for diagnosing a bone and/or joint disease comprising contacting a sample with the antisense polynucleotide according to claim 23.

76. (new): The method according to claim 75, wherein the bone and/or joint disease is osteoarthritis.

77. (new): A method for diagnosing a bone and/or joint disease comprising contacting a sample with the RNAi molecule according to claim 24.

78. (new): The method according to claim 77, wherein the bone and/or joint disease is osteoarthritis.

79. (new): A method for diagnosing a bone and/or joint disease comprising contacting a sample with the antibody according to claim 25.

80. (new): The method according to claim 79, wherein the bone and/or joint disease is osteoarthritis.

81. (new): A method for diagnosing a bone and/or joint disease comprising contacting a sample with and the compound according to claim 30.

82. **(new):** The method according to claim 81, wherein the bone and/or joint disease is osteoarthritis.

83. **(new):** A method for preparing an animal model of a bone and/or joint disease comprising administering at least one of the transformant according to claim 19.

84. **(new):** The method for preparing an animal model according to claim 83, wherein the bone and/or joint disease is osteoarthritis.

85. **(new):** A method for preparing an animal model of a bone and/or joint disease comprising administering at least one of the polypeptide according to any one of claims 20 to 22.

86. **(new):** The method for preparing an animal model according to claim 85, wherein the bone and/or joint disease is osteoarthritis.

87. **(new):** A method for preparing an animal model of a bone and/or joint disease comprising administering at least one of the antisense polynucleotide according to claim 23.

88. **(new):** The method for preparing an animal model according to claim 87, wherein the bone and/or joint disease is osteoarthritis.

89. (new): A method for preparing an animal model of a bone and/or joint disease comprising administering at least one of the RNAi molecule according to claim 24.

90. (new): The method for preparing an animal model according to claim 89, wherein the bone and/or joint disease is osteoarthritis.

91. (new): A method for preparing an animal model of a bone and/or joint disease comprising administering at least one of the antibody according to claim 25.

92. (new): The method for preparing an animal model according to claim 91, wherein the bone and/or joint disease is osteoarthritis.

93. (new): A method for preparing an animal model of a bone and/or joint disease comprising administering at least one of the compound according to claim 30.

94. (new): The method for preparing an animal model according to claim 93, wherein the bone and/or joint disease is osteoarthritis.